REMARKS

Claims 1-5, 8, 10, and 37-51 were pending in the subject application. By this Amendment, applicants have canceled Claims 2 and 5 without prejudice or disclaimer and amended Claims 1, 3-4, 37-40, and 49-51. The amendment places the application in condition for allowance or in better form for appeal. Upon entry of the Amendment, Claims 1, 3-4, 8, 10 and 37-51 will be pending and under examination.

Applicants maintain that the amendments do not raise an issue of new matter. Support for the amendments can be found at least in the previous version of the claims. Since the Examiner has not accorded patentable weight to dose ranges specified in the claims, dose ranges have been moved from independent Claims 1 and 4 to dependent Claims 49 and 50. Accordingly, entry of the amendments is respectfully requested.

Rejections under 35 U.S.C. §112, Second Paragraph

Claims 2-3, 38-39 and 50-51 are rejected under 35 U.S.C. §112, second paragraph, because the claims recite "BRL-47672." The Examiner indicated that the claim scope is uncertain because a trade name cannot be used to properly identify any particular material.

In the reply to the last Office Action, applicants submitted two journal articles that illustrate the structure of BRL-47672 (Sillence, M.N. et al. Am. J. Physiol. 268: E159-E167, 1995; and Jones, S.W. et al. J. Pharmacol. Exp. Ther. 311(3):1225-1231, 2004). In the current Office Action, the Examiner indicated that information from journal articles is not generally considered as "well-known" to one of ordinary skill in the art. Applicants strongly disagree with the Examiner's position that articles from two leading, peer-reviewed, internationally available journals, such as the American Journal of Physiology and the Journal of Pharmacology and Experimental Therapeutics, would not

be well-known to those working in this field, especially since the tem "BRL-47672" appears in the title of each of the two articles. Nevertheless, in order to advance the prosecution of the subject application, applicants have hereinabove amended Claims 2-3, 38-39 and 50-51 to delete the term "BRL-47672," thereby rendering this rejection moot.

Rejections under 35 U.S.C. §102

Claims 1, 5, 8, 41-44, and 47-49 stand rejected under 35 U.S.C. §102(a) as anticipated by Murphy et al. (Arch. Phys. Med. Rehabil. 80(10): 1264-67, 1999).

In reply, Claim 1 has hereinabove been amended to add the features recited in Claim 2, which is not rejected over Murphy et al. Applicants maintain that this amendment obviates this rejection with respect to Claim 1.

Dependent Claims 42, 43 and 47 all depend from, incorporate the limitations of, and further limit independent Claim 1, which has been amended as described above. Accordingly, applicants maintain that Claims 42, 43 and 47 are patentable over Murphy et al.

Dependent Claims 8, 41, 44, and 48 all depend from, incorporate the limitations of, and further limit independent Claim 37, which the Examiner indicated is patentable over Murphy et al. Accordingly, applicants maintain that Claims 8, 41, 44 and 48 are patentable over Murphy et al.

Claim 49 has hereinabove been amended to depend from independent Claim 4, which is not rejected over Murphy et al.

Claim 5 has hereinabove been canceled, thereby rendering this rejection moot with respect to Claim 5.

Accordingly, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejections under 35 U.S.C. §103(a)

A. Claim 10 is rejected under 35 U.S.C. §103(a) as not patentable over Murphy et al. (Arch. Phys. Med. Rehabil. 80(10): 1264-67, 1999).

Applicants respectfully traverse this rejection.

In the current Office Action, the Examiner states that independent Claim 37 is patentable over Murphy et al. under both 35 U.S.C. §102 and §103.

Dependent Claim 10, depends from, incorporates the limitations of, and further limits independent Claim 37.

Accordingly, in view of the above remarks, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

B. Claims 1-5, 8, 10, and 37-51 stand rejected under 35 U.S.C. §103(a) as not patentable over Stone et al. (U.S. Patent No. 5,281,607).

Applicants respectfully traverse this rejection.

The cited reference does not teach or suggest all the limitations of the claims, as is required for an obviousness rejection (MPEP §2143).

Stone et al. teach the treatment of neurodegenerative diseases and/or central nervous system trauma using substances that increase expression of nerve growth factor (NGF) in the central nervous system, where the substances are selected from a β-adrenergic agonist, an α1-adrenergic agonist, and/or an α2-adrenergic antagonist. Alpha2-adrenergic antagonists are preferred. (See Column 1, lines 13-17, and Column 3,

lines 39-47.)

In contrast, the present invention is directed to methods of increasing locomotor function and/or neuromuscular strength in a mammalian patient with spinal cord contusion injury or motor neuron degeneration comprising administering a β_2 adrenergic agonist to the patient.

Stone et al. do not teach methods "to increase locomotor function" as specified in all the claims of the subject invention.

Stone et al. also do not teach rehabilitation following "spinal cord contusion injury" or "injury to the lower thoracic spine."

Stone et al. teach the use of β-adrenergic agonists, but do not specifically indicate the use of $\underline{\beta_2}$ adrenergic agonists. Stone et al. list some individual β-adrenergic agonists without regard for whether the β-adrenergic agonist is a β_1 adrenergic agonist or a β_2 adrenergic agonist (see Column 4, lines 22-25). It would not have been obvious from Stone et al. to use a $\underline{\beta_2}$ adrenergic agonist as opposed to a β_1 adrenergic agonist as is required for the instant invention.

In addition, Stone et al. fail to provide any working examples to show that any agents, let a β-adrenergic agonist, has any therapeutic or functional effect. The only working example provided by Stone et al. is a demonstration that the α2 antagonist yohimbine increases NGF mRNA in the hippocampus of the brains of rats. However, it is well known that mRNA levels can be very different from protein levels. Such differences may be due, for example, to regulation of protein translation and/or protein turnover in the cell. As previously discussed, a subsequent 1994 publication by Stone and colleagues reported that, even though yohimbine increased NGF mRNA levels three fold, NGF protein levels were unaltered in the brain *in vivo* (Stone et al., Neurosci. Lett. 167: 11-13, 1994). Accordingly, the preferred treatment embodiment described in U.S. Patent

No. 5,281,607 (Stone et al.) failed to have a functional effect because the treatment failed to alter levels of NGF protein. The 1994 report by Stone et al. also recounts an example of another substance (kainic acid) that increases NGF mRNA levels in the brain but fails to increase NGF protein levels. Rather, kainic acid actually decreased NGF protein levels in the brain while increasing NGF mRNA levels (see last paragraph of Stone et al., Neurosci. Lett. 167: 11-13, 1994). Inspection of the data presented by Stone et al. also shows that NGF protein levels in the brain appear to decrease 48 hours after treatment with the α2 antagonist yohimbine (see Figure 2 on page 12 of Stone et al., Neurosci. Lett. 167: 11-13, 1994).

In view of the 1994 report by Stone et al. that the preferred treatment proposed in U.S. Patent No. 5,281,607 fails to increase NGF protein level in the brain, the skilled artisan would have reasonable doubts regarding the therapeutic effectiveness of any similar treatment mentioned in the Stone et al. patent, which also fails to provide any evidence that any β-adrenergic agonist has any therapeutic effect. Accordingly, Stone et al. do not provide the skilled artisan with the reasonable expectation of success required for a rejection under 35 U.S.C. §103 (MPEP §2143). At best, Stone et al. present an invitation to experiment.

In view of the remarks made hereinabove, applicants submit that the claimed invention is patentable over Stone et al. Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

CONCLUSIONS

In light of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the rejections in the March 15, 2005 Final Office Action and earnestly solicit passage of the pending claims to allowance. Should there be any minor matters preventing allowance of the subject application, the Examiner is requested to telephone the undersigned attorney.

No fee is deemed necessary in connection with the filing of this reply. However, if any unanticipated payment is required to maintain the pendency of this application, authorization is given to withdraw the amount of any such fee from Deposit Account No. 01-1785.

Respectfully submitted,

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